Jan DELAVAL
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Access DB# 55292

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Joseph Young Examiner #: 79813 Date: 1/27/03
Art Unit: 1623 Phone Number 308-6605-1201 Serial Number: 10/014,472
Mail Box and Bldg/Room Location: 8D41 Results Format Preferred (circle): PAPER DISK E-MAIL
8B19

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Exanopeptin analogs and methods of its use

Inventors (please provide full names): KERN, Christopher; HOERBER, Christine
BARTNIK, Eckart; HAUS-SEUFFERT, Philipp

Earliest Priority Filing Date: 12/16/00

For Sequence Searches Only *Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

Attached: 1) B.b Sheet; 2) Assignment Info; 3) Pending Claims (1-8 only); 4) Abstract.

Please search claims 1-3.

Thanks!

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CM1 1E07 – 703-308-4498
jan.delaval@uspto.gov

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STAFF USE ONLY	Type of Search	Vendors and cost where applicable
Searcher:	NA Sequence (#)	STN ✓
Searcher Phone #: 4498	AA Sequence (#)	Dialog
Searcher Location:	Structure (#)	Questel/Orbit
Date Searcher Picked Up: 1/31/03	Bibliographic ✓	Dr.Link
Date Completed: 1/31/03	Litigation	Lexis/Nexis
Searcher Prep & Review Time:	Fulltext	Sequence Systems
Clerical Prep Time: 15	Patent Family	WWW/Internet
Online Time: +91	Other	Other (specify)

PTO-1590 (8-01)

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=> fil reg
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Property values tagged with IC are from the ZIC/VINITI data file
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STRUCTURE FILE UPDATES:   30 JAN 2003  HIGHEST RN 483965-49-7
DICTIONARY FILE UPDATES:  30 JAN 2003  HIGHEST RN 483965-49-7

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> d ide  can tot l1

L1   ANSWER 1 OF 2  REGISTRY  COPYRIGHT 2003 ACS
RN   9041-08-1  REGISTRY
CN   Heparin, sodium salt (8CI, 9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   Alfa 87-120
CN   Alfa 87-163
CN   Alfa 87-198
CN   Alfa 87-81
CN   Alfa 88-247
CN   Ardeparin sodium
CN   Bemiparin sodium
CN   Clexan
CN   Dalteparin sodium
CN   Deligoparin sodium
CN   Depo-Heparin
CN   Enoxaparin sodium
CN   Fragmin
CN   Fragmin IV
CN   H 2149
CN   Hed-Heparin
CN   Hepalean
CN   Heparin sodium
CN   Hepathrom
CN   Inno-Hep
CN   Kabi 2165
CN   LHN 1
CN   Lioton 1000
CN   Liquaemin sodium
CN   Liquemin
CN   Logiparin
CN   Lovenox
CN   Minolteparin sodium
CN   Normiflo
CN   OP 2000
CN   Parnaparin sodium
CN   PK 10169
CN   Pularin
```

Jan Delaval
Reference Librarian
Biotechnology & Chemical Library
CM1 1E07 – 703-308-4498
jan.delaval@uspto.gov

CN Reviparin sodium
CN RO 11
CN RP 54563
CN Sodium acid heparin
CN Sodium heparin
CN Sodium heparinate
CN Tinzaparin sodium
CN WY 90493RD
DR 12656-11-0, 101921-26-0, 102785-31-9
MF Unspecified
CI PMS, COM, MAN
PCT Manual registration, Polyester, Polyester formed
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CAPLUS, CBNB, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DETHERM*, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PHAR, PHARMASEARCH, PROMT, RTECS*, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, TSCA**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
1031 REFERENCES IN FILE CA (1962 TO DATE)
78 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1034 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:69342

REFERENCE 2: 138:66690

REFERENCE 3: 138:61397

REFERENCE 4: 138:61375

REFERENCE 5: 138:49698

REFERENCE 6: 138:33098

REFERENCE 7: 138:11261

REFERENCE 8: 138:1961

REFERENCE 9: 138:221

REFERENCE 10: 137:379827

L1 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2003 ACS
RN 9005-49-6 REGISTRY
CN Heparin (8CI, 9CI) (CA INDEX NAME)
OTHER NAMES:
CN .alpha.-Heparin
CN Bemiparin
CN Certoparin
CN Clexane
CN Clivarin
CN Clivarine
CN CY 216
CN CY 222
CN Dalteparin
CN **Enoxaparin**
CN Fluxum
CN FR 860
CN Fragmin A

CN Fragmin B
CN Fraxiparin
CN Heparin subcutan
CN Heparin sulfate
CN Heparinic acid
CN KB 101
CN Multiparin
CN Novoheparin
CN OP 386
CN OP 622
CN Pabyrn
CN Parnaparin
CN Parvoparin
CN Reviparin
CN Sandoparin
CN Sublingula
CN Tinzaparin
CN Vetren
CN Vitrum AB
DR 9075-96-1, 11078-24-3, 11129-39-8, 104521-37-1, 37324-73-5, 91449-79-5
MF Unspecified
CI PMS, COM, MAN
PCT Manual registration, Polyester, Polyester formed
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PHAR, PHARMASEARCH, PIRA, PROMT, RTECS*, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
19746 REFERENCES IN FILE CA (1962 TO DATE)
1876 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
19758 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:78563

REFERENCE 2: 138:78444

REFERENCE 3: 138:78330

REFERENCE 4: 138:78292

REFERENCE 5: 138:78289

REFERENCE 6: 138:69395

REFERENCE 7: 138:68799

REFERENCE 8: 138:66705

REFERENCE 9: 138:66434

REFERENCE 10: 138:66401

=> d his

(FILE 'HOME' ENTERED AT 15:54:18 ON 31 JAN 2003)
SET COST OFF

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     FILE 'REGISTRY' ENTERED AT 15:54:31 ON 31 JAN 2003
                E ENOXAPARIN/CN
L1            2 S E3,E4

     FILE 'MEDLINE' ENTERED AT 15:55:05 ON 31 JAN 2003
L2        36431 S L1
L3         1039 S ENOXAPARIN?
L4        55221 S HEPARIN
L5          832 S L3 AND L2,L4
L6         1039 S L3,L5
                E ENOXAPARIN/CT
L7          677 S E3-E20
                E E3+ALL
L8          677 S E65+NT
L9          128 S CLEXANE OR EMT 966 OR EMT 967 OR EMT966 OR EMT967 OR LOVENOX
L10        1091 S L3,L7-L9
                E ENOXAPARIN/CN
L11         677 S E3
L12        1091 S L10,L11
                E MATRIX METALLOPROTEASE/CT
                E E15+ALL
L13        6626 S E11+NT
L14        7779 S MATRIX()(METALLOPROTEINASE OR METALLOPROTEASE OR METALLO()(PR
L15        2831 S MMP8 OR MMP2 OR MMP()(8 OR 2)
L16        3015 S NEUTROPHIL COLLAGENASE OR AGGRECANASE OR HADAMTS 1 OR GELATIN

     FILE 'REGISTRY' ENTERED AT 16:00:18 ON 31 JAN 2003
                E AGGRECANASE/CN
L17           1 S E3
                E HADAMTS/CN
                E GELATINASE/CN
L18           1 S E16
                E NEUTROPHIL COLLAGENASE/CN
                E COLLAGENASE/CN
L19           1 S E3
L20           3 S NEUTROPHIL(L)COLLAGENASE
                E MATRIX METALLOPROTEINASE/CN
L21           1 S E3
L22         406 S MATRIX(L)(METALLOPROTEINASE OR METALLOPROTEASE)

     FILE 'MEDLINE' ENTERED AT 16:02:25 ON 31 JAN 2003
L23          11 S L17-L22
L24        9723 S L13-L16,L23
L25           0 S L12 AND L24
                E DEGENERATIVE JOINT/CT
                E JOINT DISEASE/CT
                E E5+ALL
L26          20 S C5./CT AND L12
                E JOINT/CT
                E JOINTS/CT
                E E3+ALL
L27          22 S L12 AND A2./CT
                E CONNECTIVE TISSUE/CT
L28          10 S L12 AND E3+NT
L29           1 S E5+NT AND L12
                E WOUND/CT
L30           2 S E6+NT AND L12
L31           0 S E19+NT AND L12
L32          55 S E68+NT AND L12
                E PERIODONTAL DISEASE/CT
L33           0 S E4+NT AND L12
L34           1 S C7./CT AND L12
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L35           1 S L12 AND (A14.254. OR G10.549. OR E6. OR A12.300. OR A12.383.)
                E BONE METABOLISM/CT
                E "BONE AND BONES"/CT
L36          10 S E3+NT AND L12
                E BONE DISEASE/CT
L37          17 S E9+NT AND L12
L38          32 S A11./CT AND L12
                E LOCOMOTER/CT
L39           1 S E4+NT AND L12
                E E5+ALL
L40           0 S E2+NT AND L12
                E OSTEOARTHROSE/CT
                E E4+ALL
L41           1 S E2+NT AND L12
                E SPONDYLOSE/CT
                E E4+ALL
L42           0 S E2+NT AND L12
                E CHONDROLYSIS/CT
L43           0 S E3/BI AND L12
                E COLLAGENOSE/CT
L44           0 S E3/BI AND L12
                E INFLAMMATION/CT
L45           3 S E3+NT AND L12
L46          30 S ?INFLAM? AND L12
                E CHRONIC ARTHRIT/CT
                E E4+ALL
L47           0 S E2+NT AND L12
                E ARTHROPATH/CT
                E E6+ALL
L48           0 S E2+NT AND L12
                E MYALGIA/CT
                E E4+ALL
L49           0 S E2+NT AND L12
L50           0 S E8+NT AND L12
L51           0 S L12 AND DEGEN?(L)JOINT
L52           0 S L12 AND CONNECTIVE TISSUE
L53           1 S L12 AND WOUND?(L)HEAL?
L54           0 S L12 AND ?PERIODONT?
L55           0 S L12 AND LOCOMOTER
L56           0 S L12 AND LOCOMOTION
L57           2 S L12 AND BONE(L)METABOL?
L58          32 S L12 AND (OSTEOARTHR? OR SPONDYLO? OR CHONDROLYS? OR COLLAGENO
L59         140 S L26-L58
L60          21 S L59 NOT AB/FA
L61         119 S L59 NOT L60
L62           0 S L61 AND L24
L63           0 S L61 AND MMP?
L64          75 S L61 AND L7
L65          57 S L61 AND L7/MAJ
L66          51 S L65 AND PY<=2001
                SEL DN AN 10 21 51
L67           3 S E1-E9
L68           5 S L34,L35,L67 AND L12-L16,L23-L67
L69          18 S L64 NOT L65-L68
L70          44 S L61 NOT L64-L69
                SEL DN AN 2
L71           1 S L70 AND E10-E12
L72           6 S L68,L71 AND L12-L16,L23-L71

     FILE 'REGISTRY' ENTERED AT 16:35:39 ON 31 JAN 2003

=> fil medline
FILE 'MEDLINE' ENTERED AT 16:35:53 ON 31 JAN 2003
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FILE LAST UPDATED: 30 JAN 2003 (20030130/UP). FILE COVERS 1958 TO DATE.

On June 9, 2002, MEDLINE was reloaded. See HELP RLOAD for details.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2003 vocabulary. See http://www.nlm.nih.gov/mesh/summ2003.html for a description on changes.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d l72 all tot

L72 ANSWER 1 OF 6 MEDLINE
AN **2002718563** IN-PROCESS
DN **22368648** PubMed ID: **12480085**
TI A synthetic heparin-mimicking polyanionic compound inhibits central nervous system **inflammation**.
AU Irony-Tur-Sinai Michal; Vlodavsky Israel; Ben-Sasson Shmuel A; Pinto Florence; Sicsic Camille; Brenner Talma
CS Laboratory of Neuroimmunology, Department of Neurology, Hadassah University Hospital and Hebrew University Medical School, P.O. Box 12000, 91120, Jerusalem, Israel.
SO JOURNAL OF THE NEUROLOGICAL SCIENCES, (2003 Jan 15) 206 (1) 49-57. Journal code: 0375403. ISSN: 0022-510X.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS IN-PROCESS; NONINDEXED; Priority Journals
ED Entered STN: 20021218
Last Updated on STN: 20021218
AB The immunomodulating capacity of heparin led us to test the effect of the synthetic heparin-mimicking and low anticoagulant compound RG-13577 on the course of experimental autoimmune encephalomyelitis (EAE) and central nervous system (CNS) **inflammation**. EAE was induced in SJL mice by inoculation with whole mouse spinal cord homogenate. RG-13577, delivered intraperitoneally, inhibited the clinical signs of acute EAE and markedly ameliorated **inflammation** in the spinal cord, primarily by inhibiting heparanase activity in lymphocytes and astrocytes and thus impairing lymphocyte traffic. RG-13577 treatment was effective when started on day of disease induction or day 7 after induction. The low molecular weight heparin, **enoxaparin**, tested under the same conditions, exerted only a minor insignificant inhibitory effect. RG-13577 also inhibited the tyrosine phosphorylation of several proteins, particularly Erk1 and Erk2 of the MAP kinase signaling pathways associated with **inflammation** and cell proliferation. RG-13577 blocked the activity of sPLA(2) and inhibited CNS PGE(2) production both in vivo and in vitro.

L72 ANSWER 2 OF 6 MEDLINE
AN **2001493430** MEDLINE
DN **21427354** PubMed ID: **11535902**
TI Thromboprophylaxis with 60 mg **enoxaparin** is safe in hip trauma surgery.
AU Thaler H W; Roller R E; Greiner N; Sim E; Korninger C
CS Trauma Center Meidling, Kundratstrasse 37, A 1120 Vienna, Austria.. drthaler@aon.at
SO JOURNAL OF TRAUMA, **(2001 Sep)** 51 (3) 518-21. Journal code: 0376373. ISSN: 0022-5282.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English

FS Abridged Index Medicus Journals; Priority Journals
EM 200109
ED Entered STN: 20010906
Last Updated on STN: 20011001
Entered Medline: 20010927
AB BACKGROUND: Little information is available concerning dosage and optimal initiation of thromboprophylactic therapy with low-molecular-weight heparin (**enoxaparin**) in nonelective hip surgery. The aim of our prospective study was to evaluate the incidence of clinically apparent deep vein thrombosis (DVT), pulmonary embolism (PE), and major hemorrhage in patients receiving thromboprophylaxis with **enoxaparin** undergoing hip surgery after hip fracture. METHOD: From 946 consecutive patients admitted with hip fractures, 897 were operated on and received **enoxaparin** according to the following regimen: Preoperative heparinization from time of admission onwards. Administration of 60 mg **enoxaparin**, in two doses (20 and 40 mg subcutaneously), during the first 5 days postoperatively. Prophylaxis for a minimum of 5 weeks (40 mg daily). RESULTS: Clinical signs of DVT were present in 37 patients (4.2%), who all underwent venography. In five patients, DVT was confirmed (0.6%). None of these patients suffered from PE. Another four patients (0.4%) developed clinical signs of PE, and suspected diagnosis was confirmed by computed tomographic scan in two (0.2%). No deaths because of PE were observed. Major hemorrhage occurred in 42 patients (4.7%), there was one death from hemorrhage caused by an intracerebral event. No case of heparin-induced thrombocytopenia type II was observed. CONCLUSION: Thromboprophylaxis with 60 mg **enoxaparin** daily, in split doses, starting before surgery, is safe and appropriate in patients with hip fractures. Clinically apparent DVT and PE are rarely observed, and bleeding complications are comparable to those occurring with a conventional thromboprophylactic regimen.
CT Check Tags: Female; Human; Male
Adult
Aged
Aged, 80 and over
Anticoagulants: AD, administration & dosage
*Anticoagulants: TU, therapeutic use
Comorbidity
Drug Administration Schedule
Enoxaparin: AD, administration & dosage
***Enoxaparin: TU, therapeutic use**
***Femoral Neck Fractures: SU, surgery**
Middle Age
Phlebography
*Postoperative Complications: PC, prevention & control
Pulmonary Embolism: ET, etiology
Reoperation
Septicemia: ET, etiology
*Venous Thrombosis: PC, prevention & control
CN 0 (Anticoagulants); **0 (Enoxaparin)**

L72 ANSWER 3 OF 6 MEDLINE
AN 2001483050 MEDLINE
DN 21417531 PubMed ID: 11526584
TI Outpatient use of low-molecular weight heparin in an anticoagulated patient requiring oral surgery: case report.
CM Comment in: J Oral Maxillofac Surg. 2002 Mar;60(3):342
AU Todd D W; Roman A
SO JOURNAL OF ORAL AND MAXILLOFACIAL SURGERY, (2001 Sep) 59 (9) 1090-2; discussion 1092-3.
Journal code: 8206428. ISSN: 0278-2391.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English

FS Abridged Index Medicus Journals; Dental Journals; Priority Journals
EM 200109
ED Entered STN: 20010830
Last Updated on STN: 20021001
Entered Medline: 20010920
CT Check Tags: Case Report; Human; Male
Administration, Oral
Aged
*Ambulatory Surgical Procedures
*Anticoagulants: AD, administration & dosage
***Dental Care for Chronically Ill**
***Enoxaparin: AD, administration & dosage**
*Heart Valve Prosthesis
Injections, Subcutaneous
***Tooth Extraction**
Warfarin: AD, administration & dosage
RN 81-81-2 (Warfarin)
CN 0 (Anticoagulants); **0 (Enoxaparin)**

L72 ANSWER 4 OF 6 MEDLINE
AN **2001077378** MEDLINE
DN **21013535** PubMed ID: **11127666**
TI Thromboprophylaxis using a low molecular weight heparin delays fracture repair.
AU Street J T; McGrath M; O'Regan K; Wakai A; McGuinness A; Redmond H P
CS Department of Academic Surgery, Cork University Hospital/University College Cork, Ireland.
SO CLINICAL ORTHOPAEDICS AND RELATED RESEARCH, **(2000 Dec)** (381) 278-89.
Journal code: 0075674. ISSN: 0009-921X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200101
ED Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010111
AB Low molecular weight heparins are significantly superior to unfractionated heparin or warfarin in the prevention of thromboembolic episodes associated with orthopaedic surgery. Therapeutic doses of heparin and warfarin have been shown to delay bone repair in a rabbit model. The current study investigated the effect of prophylactic administration of a low molecular weight heparin, **enoxaparin**, on the healing of a closed rabbit rib fracture. Fracture healing was assessed using histomorphometric, histologic, and immunohistochemical methods at 3, 7, and 14 days, and biomechanical testing with torsional loading was assessed after 21 days. Bone repair was significantly attenuated at all times in animals receiving subcutaneous **enoxaparin** compared with that of the control animals. Numerous putative mechanisms for this phenomenon are discussed, and additional studies are proposed to elucidate the effects of this pharmacologically diverse group of compounds on all aspects of bone physiology and repair.
CT Check Tags: Animal; Male
*Anticoagulants: AE, adverse effects
Biomechanics
Bone and Bones: DE, drug effects
Bony Callus: PA, pathology
Disease Models, Animal
***Enoxaparin: AE, adverse effects**
***Fracture Healing: DE, drug effects**
*Postoperative Complications: PC, prevention & control
Rabbits

Rib Fractures: PA, pathology
Rib Fractures: SU, surgery
Thrombosis: PC, prevention & control
CN 0 (Anticoagulants); **0 (Enoxaparin)**

L72 ANSWER 5 OF 6 MEDLINE
AN 1998215078 MEDLINE
DN 98215078 PubMed ID: 9555795
TI Low-dose low-molecular-weight heparin (**enoxaparin**) is beneficial in lichen planus: a preliminary report.
CM Comment in: J Am Acad Dermatol. 2002 Jan;46(1):141-3
AU Hodak E; Yosipovitch G; David M; Ingber A; Chorev L; Lider O; Cahalon L; Cohen I R
CS Department of Dermatology, Rabin Medical Center, Beilinson Campus, Petah Tikva, and Sackler Faculty of Medicine, Tel Aviv University, Israel.
SO JOURNAL OF THE AMERICAN ACADEMY OF DERMATOLOGY, **(1998 Apr)** 38 (4) 564-8.
Journal code: 7907132. ISSN: 0190-9622.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199805
ED Entered STN: 19980514
Last Updated on STN: 20020911
Entered Medline: 19980505
AB BACKGROUND: Low-dose heparin devoid of anticoagulant activity inhibits T-lymphocyte heparanase activity, which is crucial in T-cell migration to target tissues. OBJECTIVE: The purpose of this study was to assess the efficacy of low-dose **enoxaparin** (**Clexane**), a low-molecular-weight heparin, as monotherapy in lichen planus. METHODS: Included in the study were 10 patients with widespread histopathologically proven lichen planus (LP) associated with intense pruritus of several months' duration. Patients were given 3 mg **enoxaparin**, subcutaneously once weekly; three patients received four injections, and seven patients received six injections. RESULTS: In nine patients the itch disappeared within 2 weeks. Within 4 to 10 weeks in eight of these patients, there was complete regression of the eruption with residual **postinflammatory** hyperpigmentation; in one patient, there was marked improvement. In one patient, no effect was observed. Of the four patients who also had oral LP, only one showed improvement. No side effects were observed in any of the patients. CONCLUSION: These findings indicate that **enoxaparin** may be a simple, effective treatment for cutaneous LP.
CT Check Tags: Female; Human; Male
Adult
Aged
Biopsy
***Enoxaparin: AD, administration & dosage**
Enoxaparin: TU, therapeutic use
Follow-Up Studies
*Lichen Planus: DT, drug therapy
Lichen Planus: PA, pathology
Lichen Planus, Oral: DT, drug therapy
Lichen Planus, Oral: PA, pathology
Middle Age
Skin: PA, pathology
Time Factors
Treatment Outcome
CN **0 (Enoxaparin)**

L72 ANSWER 6 OF 6 MEDLINE
AN **94055646** MEDLINE

DN **94055646** PubMed ID: **8237316**
TI Increased blood loss after preoperative NSAID. Retrospective study of 186 hip arthroplasties.
AU Fauno P; Petersen K D; Husted S E
CS Department of Orthopedics E, University Hospital of Arhus, Denmark.
SO ACTA ORTHOPAEDICA SCANDINAVICA, **(1993 Oct)** 64 (5) 522-4.
Journal code: 0370352. ISSN: 0001-6470.
CY Denmark
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199312
ED Entered STN: 19940117
Last Updated on STN: 19940117
Entered Medline: 19931222
AB We have evaluated bleeding during and after hip replacement in 186 patients in relation to preoperative intake of nonsteroidal anti-**inflammatory** drugs (NSAID) combined with low molecular weight heparin. NSAID was associated with increased preoperative bleeding and blood transfusion requirements.
CT Check Tags: Female; Human; Male
Aged
Anti-Inflammatory Agents, Non-Steroidal: AE, adverse effects
Anti-Inflammatory Agents, Non-Steroidal: TU, therapeutic use
*Aspirin: AE, adverse effects
Aspirin: TU, therapeutic use
*Blood Loss, Surgical
Blood Loss, Surgical: PC, prevention & control
***Enoxaparin: AE, adverse effects**
Enoxaparin: TU, therapeutic use
*Hip Prosthesis: AE, adverse effects
Hip Prosthesis: MT, methods
Middle Age
*Premedication: AE, adverse effects
Retrospective Studies
RN 50-78-2 (Aspirin)
CN 0 (Anti-**Inflammatory** Agents, Non-Steroidal); **0 (Enoxaparin)**

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 17:50:25 ON 31 JAN 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 31 Jan 2003 VOL 138 ISS 6
FILE LAST UPDATED: 30 Jan 2003 (20030130/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all tot l137

L137 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2003 ACS
AN **2002:465826** HCAPLUS
DN **137:28331**
TI Use of **low-molecular-weight heparin** for treating osteoarthritis and other diseases
IN **Kern, Christopher; Hoerber, Christine; Bartnik, Eckart; Haus-Seuffert, Philipp**
PA Aventis Pharma Deutschland G.m.b.H., Germany
SO PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DT Patent
LA German
IC ICM A61K031-715
ICS A61K031-70; A61P019-02
CC **1-12** (Pharmacology)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002047696	A1	20020620	WO 2001-EP14261	20011205
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2002021935	A5	20020624	AU 2002-21935	20011205
	US 2002128226	A1	20020912	US 2001-14472	20011214
PRAI	DE 2000-10063006	A	20001216		
	WO 2001-EP14261	W	20011205		

AB The invention discloses the use of low mol. **heparin** for producing medicaments for the prophylaxis and treatment of diseases in the course of which increased activity of at least one of the **matrix metalloproteinases neutrophil collagenase, aggrecanase**, hADAMTSI and **gelatinase A** are involved.
ST **matrix metalloproteinase** disease treatment **low mol wt heparin**; osteoarthritis treatment **low mol wt heparin**
IT **Arthritis**
(chronic and acute; **low-mol.-wt. heparin** for treating **osteoarthritis** and other diseases)
IT **Cartilage**
(degeneration; **low-mol.-wt. heparin** for treating osteoarthritis and other diseases)
IT **Connective tissue**
Joint, anatomical
Periodontium
(**disease**; **low-mol.-wt. heparin** for treating osteoarthritis and other **diseases**)
IT **Wound healing**
(disorder; **low-mol.-wt. heparin** for treating osteoarthritis and other diseases)
IT **Joint, anatomical**
(immobilized; **low-mol.-wt. heparin** for treating osteoarthritis and other **diseases**

)
IT Drug delivery systems
(inhalants; **low-mol.-wt. heparin**
for treating osteoarthritis and other diseases)
IT Drug delivery systems
(injections, i.p.; **low-mol.-wt.**
heparin for treating osteoarthritis and other diseases)
IT Drug delivery systems
(injections, i.v.; **low-mol.-wt.**
heparin for treating osteoarthritis and other diseases)
IT Drug delivery systems
(injections, intraarticular; **low-mol.-wt.**
heparin for treating osteoarthritis and other diseases)
IT Drug delivery systems
(injections, s.c.; **low-mol.-wt.**
heparin for treating osteoarthritis and other diseases)
IT **Anti-inflammatory agents**
Antiarthritics
Chondrocyte
Human
Musculoskeletal diseases
Osteoarthritis
Test kits
(**low-mol.-wt. heparin** for
treating osteoarthritis and other diseases)
IT **Joint, anatomical**
(meniscus, injury; **low-mol.-wt.**
heparin for treating osteoarthritis and other **diseases**
)
IT **Muscle, disease**
(**myalgia; low-mol.-wt.**
heparin for treating osteoarthritis and other diseases)
IT Drug delivery systems
(oral; **low-mol.-wt. heparin** for
treating osteoarthritis and other diseases)
IT **Bone, disease**
(**osteopenia; low-mol.-wt.**
heparin for treating osteoarthritis and other diseases)
IT **Bone**
(patella, **injury; low-mol.-wt.**
heparin for treating osteoarthritis and other diseases)
IT Drug delivery systems
(rectal; **low-mol.-wt. heparin**
for treating osteoarthritis and other diseases)
IT **Ligament**
(torn; **low-mol.-wt. heparin** for
treating osteoarthritis and other diseases)
IT Drug delivery systems
(transdermal; **low-mol.-wt.**
heparin for treating osteoarthritis and other diseases)
IT **Spinal column**
(vertebra, **spondylosis; low-mol.-**
wt. heparin for treating osteoarthritis and other
diseases)
IT **9001-12-1, Matrix metalloproteinase** 8
79955-99-0, Matrix metalloproteinase 3
141907-41-7, Matrix metalloproteinase
146480-35-5, Gelatinase A 147172-61-0
, Aggrecanase 241475-68-3, Metalloproteinase ADAMTS1
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**low-mol.-wt. heparin** for
treating osteoarthritis and other diseases)
IT **9005-49-6, Heparin,** biological studies

RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(**low-mol.-wt. heparin** for treating osteoarthritis and other diseases)
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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(2) Cohen, I; WO 9219249 A 1992 HCAPLUS
(3) Cohen, I; US 5686431 A 1997 HCAPLUS
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(5) Talma, E; WO 0040225 A 2000 HCAPLUS

L137 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2003 ACS
AN **2001:670210** HCAPLUS
DN **135:339008**
TI Influence of different **heparins** on bone defect healing
AU Kock, H.-J.; Werther, S.; Herrmanns, B.; Schmit-Neuerburg, K. P.
CS Experimentelle Unfallchirurgie, Universitatsklinikum GHS Essen, Germany
SO Chirurgisches Forum fuer Experimentelle und Klinische Forschung (2001) 407-408
CODEN: CFEKA7; ISSN: 0303-6227
PB Springer-Verlag
DT Journal
LA German
CC **1-8** (Pharmacology)
AB Unfractionated **heparins** in high dosage are well known to cause side effects in fracture repair and bone remodeling. **Low mol. wt. heparins**, which have gained importance in antithrombotic therapy over the last decade, have not yet been investigated in regards to their possible effects on fracture repair. In a standardized rabbit bone defect model the effect of high doses of unfractionated **heparin** (UFH, n = 10), **low mol. wt. heparin** (LMWH, n = 10) and 0.9% NaCl (control, n = 10) on bone repair after 6 wk of application were studied by fluorescence, light and electron microscopy. The results of this blind investigation revealed increased bone defects in the UFH group, compared to non-significant increases in the LMWH group. Cell structures and bone matrix in the UFH showed degenerative changes only in the UFH group. The authors conclude from these findings that high-dose UFH can cause a relevant delay in bone defect healing after 6 wk, whereas LMWH in high dosage did not show such effects. Osteoblast dysfunction seems to be a possible explanation for this effect and should be investigated further.
ST **heparin** bone defect healing antithrombotic
IT **Bone, disease**
(**defect**; influence of different **heparins** on bone **defect** healing)
IT Anticoagulants
(influence of different **heparins** on bone defect healing)
IT **9005-49-6**, Certoparin, biological studies
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(**low mol. wt.**; influence of different **heparins** on bone defect healing)
IT **9041-08-1**, Sodium **heparin**
RL: ADV (Adverse effect, including toxicity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(unfractionated; influence of different **heparins** on bone defect healing)
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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(2) Schlachetzki, J; Fortschr Med 1969, V87, P119 HCAPLUS

(3) Stinchfield, F; J Bone Joint Surg 1956, V38-A, P270

L137 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2003 ACS
AN **2001:259178** HCAPLUS
DN **135:205196**
TI **Low molecular weight heparin** therapy delays fracture healing
AU Street, J. T.; McGrath, M.; O'Regan, K.; Redmond, H. H.
CS Department of Academic Surgery, Cork University Hospital, Cork, Ire.
SO Trauma, Shock, Inflammation and Sepsis: Pathophysiology, Immune Consequences and Therapy, World Congress, 5th, Munich, Germany, Feb. 29-Mar. 4, 2000 (2000), 649-654. Editor(s): Faist, Eugen. Publisher: Monduzzi Editore, Bologna, Italy.
CODEN: 69BDIP
DT Conference
LA English
CC **1-8** (Pharmacology)
Section cross-reference(s): 14
AB **Low-mol.-wt. heparins** (LMWH) bind to vascular cells and prolonged dosage causes osteopenia. Endothelial cells and pericytes disassoc. from the fracture callus vasculature and become osteoprogenitor units. Acute exposure to fracture hematoma is cytotoxic to endothelial and bone-forming cells. The authors' hypothesised that LMWH therapy would alter callus vascular disassembly and promote interfragmentary hematoma collection thus delaying fracture healing. Using a rabbit rib fracture healing model the authors demonstrate that daily s.c. administration of a therapeutic dosage of LMWH significantly delays fracture healing at 7 and 14 days. Using histol. and immunohistochem. methods this study illustrates that LMWH therapy prolongs interfragmentary hematoma accumulation, delays vascular disassembly, attenuates osteoprogenitor unit development, and inhibits endochondral ossification and callus maturation.
ST **heparin** therapy fracture healing delay
IT **Bone, disease**
(**callus; low-mol.-wt. heparin** therapy delays fracture healing)
IT Hemorrhage
(hematoma; **low-mol.-wt. heparin** therapy delays fracture healing)
IT Bone formation
Cytotoxicity
Wound healing
(**low-mol.-wt. heparin** therapy delays fracture healing)
IT **Bone, disease**
(**osteopenia; low-mol.-wt. heparin** therapy delays fracture healing)
IT **9005-49-6, Heparin**, biological studies
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BIOL (Biological study)
(**low-mol.-wt. heparin** therapy delays fracture healing)
RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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L137 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2003 ACS

AN **2000:572630** HCAPLUS
DN **134:51186**
TI **Low-molecular-weight heparin** prophylaxis using dalteparin extended out-of-hospital vs in-hospital warfarin/out-of-hospital placebo in hip arthroplasty patients: A double-blind, randomized comparison
AU Hull, Russell D.; Pineo, Graham F.; Francis, Charles; Bergqvist, David; Fellenius, Carin; Soderberg, Karin; Holmqvist, Anna; Mant, Michael; Dear, Richard; Baylis, Barry; Mah, Andrew; Brant, Rollin
CS The North American Fragmin Trial Investigators, Thrombosis Research Unit, University of Calgary, Calgary, AB, Can.
SO Archives of Internal Medicine (2000), 160(14), 2208-2215
CODEN: AIMDAP; ISSN: 0003-9926
PB American Medical Association
DT Journal
LA English
CC **1-8** (Pharmacology)
AB No randomized trials have directly evaluated the need for extended out-of-hospital thromboprophylaxis for patients who have hip arthroplasty in the United States or Canada. The uncertainty as to the need for extended prophylaxis in North American patients is complicated by early hospital discharge, resulting in a short thromboprophylaxis interval. To resolve this uncertainty, we performed a randomized double-blind trial in 569 patients who underwent hip arthroplasty comparing the use of dalteparin sodium started immediately before surgery or early after surgery and extended out-of-hospital to an overall interval of 35 days with the use of warfarin sodium in-hospital and placebo out-of-hospital. For patients with interpretable venograms in the preoperative, postoperative, and combined dalteparin groups, new proximal vein thrombosis out-of-hospital was obsd. in 1.3%, 0.7% (P=.04), and 1.0% (P=.02) of patients, resp., compared with 4.8% in the in-hospital warfarin/out-of-hospital placebo group. The resp. overall cumulative frequencies of all deep vein thrombosis were 30 (17.2%) of 174 patients (P<.001), 38 (22.2%) of 171 (P=.003), and 68 (19.7%) of 345 (P<.001) in the dalteparin groups compared with 69 (36.7%) of 188 for the in-hospital warfarin/out-of-hospital placebo group. For proximal deep vein thrombosis, the resp. frequencies were 5 (3.1%) of 162 (P=.02), 3 (2.0%) of 151 (P=.007), and 8 (2.6%) of 313 (P=.002) compared with 14 (9.2%) of 153. No major bleeding occurred during the extended prophylaxis interval. Extended dalteparin prophylaxis resulted in significantly lower frequencies of deep vein thrombosis compared with in-hospital warfarin therapy. Despite in-hospital thromboprophylaxis, patients having hip arthroplasty in the United States and Canada remain at moderate risk out-of-hospital. The no. needed to treat provides a public health focus; only 24 to 28 patients require extended prophylaxis to prevent 1 new out-of-hospital proximal vein thrombosis. Recent studies demonstrate that asymptomatic deep vein thrombi cause the postphlebitic syndrome; thus, extended out-of-hospital prophylaxis will lessen the burden to both the patient and society.
ST anticoagulant **heparin** dalteparin warfarin hip arthroplasty
IT **Joint, anatomical**
(arthroplasty, hip; **low-mol.-wt. heparin** prophylaxis using dalteparin extended out-of-hospital vs in-hospital warfarin/out-of-hospital placebo in hip arthroplasty patients)
IT **Hip**
(arthroplasty; **low-mol.-wt. heparin** prophylaxis using dalteparin extended out-of-hospital vs in-hospital warfarin/out-of-hospital placebo in hip arthroplasty patients)
IT Anticoagulants
Thrombosis
(**low-mol.-wt. heparin**

prophylaxis using dalteparin extended out-of-hospital vs in-hospital warfarin/out-of-hospital placebo in hip arthroplasty patients)

IT Vein
(phlebitis; **low-mol.-wt. heparin**
prophylaxis using dalteparin extended out-of-hospital vs in-hospital warfarin/out-of-hospital placebo in hip arthroplasty patients)

IT 129-06-6, Warfarin sodium **9041-08-1**, Dalteparin sodium
RL: ADV (Adverse effect, including toxicity); **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(**low-mol.-wt. heparin**
prophylaxis using dalteparin extended out-of-hospital vs in-hospital warfarin/out-of-hospital placebo in hip arthroplasty patients)

IT **9005-49-6, Heparin**, biological studies
RL: ADV (Adverse effect, including toxicity); **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(**low-mol.-wt; low-mol**
.-wt. heparin prophylaxis using dalteparin extended out-of-hospital vs in-hospital warfarin/out-of-hospital placebo in hip arthroplasty patients)

RE.CNT 73 THERE ARE 73 CITED REFERENCES AVAILABLE FOR THIS RECORD

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L137 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2003 ACS
AN **1994:622000** HCAPLUS
DN **121:222000**
TI Use of **heparins** for the treatment of inflammatory or immunological diseases
IN Von Arnim, Ulrich-Christoph
PA Germany
SO PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-725
CC **1-7** (Pharmacology)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9418988	A2	19940901	WO 1994-EP506	19940222
	WO 9418988	A3	19941110		
	W: AU, CA, JP, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2156735	AA	19940901	CA 1994-2156735	19940222
	AU 9462045	A1	19940914	AU 1994-62045	19940222
PRAI	EP 1993-102750		19930222		
	WO 1994-EP506		19940222		

AB A pharmaceutical for the treatment of inflammatory or immunol. diseases comprises **heparins**, heparinoids, proteoglycans, or **low -mol.-wt. heparins** or a mixt. thereof or a combination of **low-mol.-wt. heparins** and Prostavasin. These prepns. can be used for treatment of multiple sclerosis, graft-vs.-host reaction, primary biliary cirrhosis, post-infarct syndrome, lupus erythematosus, rheumatism, migraine, hyper-IgE syndrome, neuritis, Crohn's disease, and systemic carcinomas such as leukemia and lymphoma. Thus, multiple sclerosis patients with respiratory failure who received fragmin D (**low-mol.-wt. heparin**) (5 IU/kg/day s.c.) showed a 50% decrease in no. and size of sclerotic plaques in the central nervous system (by NMR scan) and decreased dependence on a respirator.

ST **heparin** inflammation inhibitor; immunol disease treatment **heparin**; multiple sclerosis treatment **heparin**; autoimmune disease treatment **heparin**

IT **Inflammation inhibitors**
Lupus erythematosus
Multiple sclerosis
(**heparins** for treatment of inflammatory or immunol. diseases)

IT Proteoglycans, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**heparins** for treatment of inflammatory or immunol. diseases)

IT Intestine, disease
(Crohn's, **heparins** for treatment of inflammatory or immunol. diseases)

IT Immunoglobulins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(E, metabolic disorders, hyperimmunoglobulin E-recurrent infection syndrome, **heparins** for treatment of inflammatory or immunol. diseases)

IT **Inflammation inhibitors**
(**antirheumatics, heparins** for treatment of inflammatory or immunol. diseases)

IT Neoplasm inhibitors
(carcinoma, **heparins** for treatment of inflammatory or immunol. diseases)

IT Biliary tract
(disease, primary biliary cirrhosis, **heparins** for treatment of inflammatory or immunol. diseases)

IT Immunity
(disorder, **heparins** for treatment of inflammatory or immunol. diseases)

IT Transplant and Transplantation
(graft-vs.-host reaction, **heparins** for treatment of inflammatory or immunol. diseases)

IT Mucopolysaccharides, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(heparinoids, **heparins** for treatment of inflammatory or immunol. diseases)

IT Heart, disease
(infarction, post-infarct syndrome; **heparins** for treatment of inflammatory or immunol. diseases)

IT Neoplasm inhibitors
(leukemia, **heparins** for treatment of inflammatory or immunol. diseases)

IT Neoplasm inhibitors
(lymphoma, **heparins** for treatment of inflammatory or immunol.

diseases)
IT Headache
(migraine, **heparins** for treatment of inflammatory or immunol. diseases)
IT Nerve, disease
(neuritis, **heparins** for treatment of inflammatory or immunol. diseases)
IT 133310-33-5, Prostavasin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination with **low-mol.-wt. heparin; heparins** for treatment of inflammatory or immunol. diseases)
IT **9005-49-6, Heparin**, biological studies
9005-49-6D, Heparin, low-mol.-wt. 9041-08-1, Fragmin
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(**heparins** for treatment of inflammatory or immunol. diseases)

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L171 ANSWER 1 OF 2 WPIX (C) 2003 THOMSON DERWENT
AN **2002-528128** [56] WPIX
DNC **C2002-149517**
TI Treatment of diseases associated with neutrophilic collagenase,

aggrecanase, hADAMTS1 and/or gelatinase A, e.g. osteoarthritis or spondylitis, using low-molecular heparin as matrix metalloproteinase inhibitor.

DC B04

IN BARTNIK, E; HAUS-SEUFFERT, P; HOERBER, C; KERN, C

PA (BART-I) BARTNIK E; (HAUS-I) HAUS-SEUFFERT P; (HOER-I) HOERBER C; (KERN-I) KERN C; (AVET) AVENTIS PHARMA DEUT GMBH

CYC 99

PI WO 2002047696 A1 20020620 (200256)* DE 19p A61K031-715
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZM ZW
US 2002128226 A1 20020912 (200262) A61K031-727
AU 2002021935 A 20020624 (200267) A61K031-715

ADT WO 2002047696 A1 WO 2001-EP14261 20011205; US 2002128226 A1 US 2001-14472 20011214; AU 2002021935 A AU 2002-21935 20011205

FDT AU 2002021935 A Based on WO 200247696

PRAI DE 2000-10063006 20001216

IC ICM A61K031-715; A61K031-727
ICS A61K031-70; A61P019-02

AB WO 200247696 A UPAB: 20020903
NOVELTY - Low-molecular heparin (I), having an average molecular weight of 3000-10000, is used for the preparation of medicaments for the prophylaxis or therapy of diseases associated with elevated activity of at least one of the matrix metalloproteinases (MMP's) neutrophilic collagenase, aggrecanase, hADAMTS1 and gelatinase A.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for the use of ADAMTS1 for the production of a test kit for the determination of aggrecanase inhibitors (II), by incubating ADAMTS1, a substrate and (II) then determining the neoepitopes generated due to the aggrecanase activity.

ACTIVITY - Osteopathic; Antiarthritic; Vulnerary; Antiinflammatory; Analgesic.

MECHANISM OF ACTION - Matrix metalloprotease (MMP) inhibitor. **Enoxaparin** (Ia) inhibited neutrophilic collagenase (MMP-8) by 28% and gelatinase A (MMP-2) by 70% at a concentration of 1 micro g/ml.

USE - (I) is specifically used for combating degenerative joint diseases (such as osteoarthritis, spondylitis, cartilage damage after joint trauma or prolonged joint immobilization after meniscus or patella damage or torn ligaments), connective tissue disorders (such as collagenosis, wound healing deficiency or periodontal disease), chronic movement disorders (such as inflammatory, immunologically metabolically induced acute or chronic arthritis, arthropathy or myalgia) or bone metabolism disorders (all claimed).

ADVANTAGE - (I) are potent and specific inhibitors of the appropriate MMP's. In particular **enoxaparin** (Ia) strongly inhibits neutrophilic collagenase (MMP-8), aggrecanase, hADAMTS1 and gelatinase A (MMP-2), but has almost no effect on MMP's 1, 3, 13 and 14.

Dwg.0/0

FS CPI

FA AB; DCN

MC CPI: B04-C02E1; B14-C01; B14-C03; B14-C09; B14-D07C; B14-N06B; B14-N17B

TECH UPTX: 20020903
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Compounds: (I) is one or more of **enoxaparin** (Ia) (most preferred), nardroparin, dalteparin, certroparin, parnaparin, reviparin, ardeparin/RD, heparin/RDH and/or tinzaparin.

ABEX
SPECIFIC COMPOUNDS - Compounds enoxaparin (Ia), nardroparin, dalteparin, certroparin, parnaparin, reviparin, ardeparin/RD, heparin/RDH and

tinzaparin are specifically claimed as (I).

ADMINISTRATION - (I) is preferably administered by subcutaneous, intraperitoneal, intravenous or especially intraarticular injection, specifically at a dose of 0.005-200 (preferably 0.01-40) mg (or particularly a daily dose of 0.01-500 (preferably 20-100) mg in the case of enoxaparin (Ia)), although rectal, oral, inhalative or transdermal administration may also be used (all claimed).

L171 ANSWER 2 OF 2 WPIX (C) 2003 THOMSON DERWENT
AN **2000-442268** [38] WPIX
DNC **C2000-134436**
TI Use of low molecular weight heparin for treatment and prevention of motor neuron disease, e.g. amyotrophic lateral sclerosis.
DC B04
IN STUTZMANN, J M; UZAN, A; STUTZMANN, J
PA (AVET) AVENTIS PHARMA SA; (STUT-I) STUTZMANN J; (UZAN-I) UZAN A
CYC 83
PI WO 2000035462 A1 20000622 (200038)* FR 18p A61K031-727
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AU BA BB BG BR CA CN CR CU CZ DM EE GD GE HR HU ID IL IN IS JP KP KR LC LK LR LT LV MA MG MK MN MX NO NZ PL RO RU SG SI SK SL TR TT UA US UZ VN YU ZA
FR 2787329 A1 20000623 (200038) A61K031-738
AU 2000015697 A 20000703 (200046) A61K031-727
NO 2001002849 A 20010608 (200154) A61K000-00
EP 1140119 A1 20011010 (200167) FR A61K031-727
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
US 2002040013 A1 20020404 (200227) A61K031-727
JP 2002532431 W 20021002 (200279) 19p A61K031-727
ADT WO 2000035462 A1 WO 1999-FR3109 19991213; FR 2787329 A1 FR 1998-15919 19981217; AU 2000015697 A AU 2000-15697 19991213; NO 2001002849 A WO 1999-FR3109 19991213, NO 2001-2849 20010608; EP 1140119 A1 EP 1999-958308 19991213, WO 1999-FR3109 19991213; US 2002040013 A1 Cont of WO 1999-FR3109 19991213, US 2001-881267 20010614; JP 2002532431 W WO 1999-FR3109 19991213, JP 2000-587782 19991213
FDT AU 2000015697 A Based on WO 200035462; EP 1140119 A1 Based on WO 200035462; JP 2002532431 W Based on WO 200035462
PRAI FR 1998-15919 19981217
IC ICM A61K000-00; A61K031-727; A61K031-738
ICS A61P009-10; A61P025-00; A61P025-28; A61P043-00
ICA C08B037-10
AB WO 200035462 A UPAB: 20000811
NOVELTY - Use of low molecular weight heparin (I) to produce a medicine that promotes survival and/or growth of motor neurons.
ACTIVITY - Cytoprotective; neurotrophic.
A mixed culture of astrocytes and motor neurons (MN) was treated with the low molecular weight heparin **Enoxaparine** (Ia), then after 2-3 days the number of viable MN assessed from:
(i) immunoreactivity for the homoprotein Islet1/2 or for neurofilaments; and
(ii) presence of neurites longer than 10 cell diameters.
At 10 ng/ml (Ia), the mean number of MN was 196% and the mean MN survival was 120.7%, both relative to a vehicle-only control as 100%. The number of very large MN was 66 per cubic centimeters (cc) in presence of (Ia) compared with 38 per cc in a control.
MECHANISM OF ACTION - None given.
No biological data given.
USE - (I) is specifically used to treat and/or prevent motor neuron diseases, particularly amyotrophic lateral sclerosis, progressive spinal muscular atrophy and infantile muscular atrophy.

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     Dwg.0/0
FS   CPI
FA   AB; DCN
MC   CPI: B04-C02E; B14-J01; B14-J05A
TECH                UPTX: 20000811
     TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Heparin: (I) has
     molecular weight 1-10, preferably 4-5, kiloDaltons (kDa). It comprises
     oligosaccharides that have, at one end, a 2-O-sulfo-4-enopyranosuronic
     acid residue and is produced by depolymerization of a heparin ester with
     base, particularly the benzyl ester with sodium hydroxide. (I) is
     particularly used as its sodium or calcium salt.
ABEX
     SPECIFIC COMPOUNDS - Eleven different low molecular weight heparin
     molecules are claimed, e.g. enoxaparine, nadroparine and parnaparine.

     ADMINISTRATION - (I) are administered by intravenous or subcutaneous
     injection, orally, rectally, etc., typically at 0.2-0.4 mg/kg/day
     subcutaneously.


=> d his

     (FILE 'HOME' ENTERED AT 15:54:18 ON 31 JAN 2003)
               SET COST OFF

     FILE 'REGISTRY' ENTERED AT 15:54:31 ON 31 JAN 2003
               E ENOXAPARIN/CN
L1           2 S E3,E4

     FILE 'MEDLINE' ENTERED AT 15:55:05 ON 31 JAN 2003
L2       36431 S L1
L3        1039 S ENOXAPARIN?
L4       55221 S HEPARIN
L5         832 S L3 AND L2,L4
L6        1039 S L3,L5
               E ENOXAPARIN/CT
L7         677 S E3-E20
               E E3+ALL
L8         677 S E65+NT
L9         128 S CLEXANE OR EMT 966 OR EMT 967 OR EMT966 OR EMT967 OR LOVENOX
L10       1091 S L3,L7-L9
               E ENOXAPARIN/CN
L11        677 S E3
L12       1091 S L10,L11
               E MATRIX METALLOPROTEASE/CT
               E E15+ALL
L13       6626 S E11+NT
L14       7779 S MATRIX()(METALLOPROTEINASE OR METALLOPROTEASE OR METALLO()(PR
L15       2831 S MMP8 OR MMP2 OR MMP()(8 OR 2)
L16       3015 S NEUTROPHIL COLLAGENASE OR AGGRECANASE OR HADAMTS 1 OR GELATIN

     FILE 'REGISTRY' ENTERED AT 16:00:18 ON 31 JAN 2003
               E AGGRECANASE/CN
L17          1 S E3
               E HADAMTS/CN
               E GELATINASE/CN
L18          1 S E16
               E NEUTROPHIL COLLAGENASE/CN
               E COLLAGENASE/CN
L19          1 S E3
L20          3 S NEUTROPHIL(L)COLLAGENASE
               E MATRIX METALLOPROTEINASE/CN
L21          1 S E3
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L22         406 S MATRIX(L)(METALLOPROTEINASE OR METALLOPROTEASE)

     FILE 'MEDLINE' ENTERED AT 16:02:25 ON 31 JAN 2003
L23          11 S L17-L22
L24        9723 S L13-L16,L23
L25           0 S L12 AND L24
                E DEGENERATIVE JOINT/CT
                E JOINT DISEASE/CT
                E E5+ALL
L26          20 S C5./CT AND L12
                E JOINT/CT
                E JOINTS/CT
                E E3+ALL
L27          22 S L12 AND A2./CT
                E CONNECTIVE TISSUE/CT
L28          10 S L12 AND E3+NT
L29           1 S E5+NT AND L12
                E WOUND/CT
L30           2 S E6+NT AND L12
L31           0 S E19+NT AND L12
L32          55 S E68+NT AND L12
                E PERIODONTAL DISEASE/CT
L33           0 S E4+NT AND L12
L34           1 S C7./CT AND L12
L35           1 S L12 AND (A14.254. OR G10.549. OR E6. OR A12.300. OR A12.383.)
                E BONE METABOLISM/CT
                E "BONE AND BONES"/CT
L36          10 S E3+NT AND L12
                E BONE DISEASE/CT
L37          17 S E9+NT AND L12
L38          32 S A11./CT AND L12
                E LOCOMOTER/CT
L39           1 S E4+NT AND L12
                E E5+ALL
L40           0 S E2+NT AND L12
                E OSTEOARTHROSE/CT
                E E4+ALL
L41           1 S E2+NT AND L12
                E SPONDYLOSE/CT
                E E4+ALL
L42           0 S E2+NT AND L12
                E CHONDROLYSIS/CT
L43           0 S E3/BI AND L12
                E COLLAGENOSE/CT
L44           0 S E3/BI AND L12
                E INFLAMMATION/CT
L45           3 S E3+NT AND L12
L46          30 S ?INFLAM? AND L12
                E CHRONIC ARTHRIT/CT
                E E4+ALL
L47           0 S E2+NT AND L12
                E ARTHROPATH/CT
                E E6+ALL
L48           0 S E2+NT AND L12
                E MYALGIA/CT
                E E4+ALL
L49           0 S E2+NT AND L12
L50           0 S E8+NT AND L12
L51           0 S L12 AND DEGEN?(L)JOINT
L52           0 S L12 AND CONNECTIVE TISSUE
L53           1 S L12 AND WOUND?(L)HEAL?
L54           0 S L12 AND ?PERIODONT?
L55           0 S L12 AND LOCOMOTER
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L56           0 S L12 AND LOCOMOTION
L57           2 S L12 AND BONE(L)METABOL?
L58          32 S L12 AND (OSTEOARTHR? OR SPONDYLO? OR CHONDROLYS? OR COLLAGENO
L59         140 S L26-L58
L60          21 S L59 NOT AB/FA
L61         119 S L59 NOT L60
L62           0 S L61 AND L24
L63           0 S L61 AND MMP?
L64          75 S L61 AND L7
L65          57 S L61 AND L7/MAJ
L66          51 S L65 AND PY<=2001
                SEL DN AN 10 21 51
L67           3 S E1-E9
L68           5 S L34,L35,L67 AND L12-L16,L23-L67
L69          18 S L64 NOT L65-L68
L70          44 S L61 NOT L64-L69
                SEL DN AN 2
L71           1 S L70 AND E10-E12
L72           6 S L68,L71 AND L12-L16,L23-L71

     FILE 'REGISTRY' ENTERED AT 16:35:39 ON 31 JAN 2003

     FILE 'MEDLINE' ENTERED AT 16:35:53 ON 31 JAN 2003

     FILE 'HCAPLUS' ENTERED AT 16:37:17 ON 31 JAN 2003
L73         457 S L3 OR L9
L74         393 S L1 AND L73
L75         457 S L73,L74
                E ENOXAPAR
L76         415 S E1,E4-E7,E9,E10
                E ENOXA
L77         459 S L75,L76
                E KERN C/AU
L78         111 S E3-E10,E14,E24,E29,E30
                E HOERBER C/AU
L79           1 S E4
                E HORBER C/AU
L80           3 S E3,E4
                E HEORBER C/AU
                E BARTNIK E/AU
L81          66 S E3-E6
                E HAUS SEUFFERT P/AU
L82           5 S E3,E4
                E SEUFFERT/AU
L83           0 S L77 AND L78-L82
L84           1 S L1 AND L78-L82
L85        9878 S L14-L16
L86       20995 S L17-L22
L87           3 S L77 AND L85,L86
L88       41112 S L1 OR HEPARIN
L89        2641 S L88 AND (LMW OR LOW()(MOL OR MOLECUL?)()(WT OR WEIGHT))
L90        2756 S L77,L89
L91           1 S L79-L82 AND L90
L92           1 S L84,L91
L93          23 S L90 AND L85,L86
L94          11 S L93 AND (1 OR 63)/SC,SX
L95          12 S L93 NOT L94
                E ARTHRITIS/CT
L96       20295 S E3+NT
                E E3+ALL
                E E1 9+ALL
                E ARTHRITIS/CT
                E E3+ALL
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                E E19+ALL
L97          4499 S E5,E4
                E CARTILAGE/CT
                E E3+ALL
L98         14562 S E7+NT
                E CONNECTIVE TISSUE/CT
                E E3+ALL
L99        245883 S E3+NT
                E JOINT/CT
                E E6+ALL
L100         8803 S E6,E5+NT
                E E13+ALL
L101         2576 S E2+NT
                E PERIODONT/CT
                E E5+ALL
L102         2587 S E2
                E PERIODONT/CT
                E E11+ALL
L103         6922 S E8+NT
                E WOUND/CT
L104         2248 S E3+NT
L105         2299 S E9+NT
                E E6+ALL
L106         6992 S E2+NT
                E E10+ALL
L107          649 S E4
                E E7+ALL
                E E11+ALL
                E ANTIINFLAM/CT
                E E5+ALL
                E E2+ALL
L108        48208 S E4,E5,E3+NT
                E CHONDROCYT/CT
                E E4+ALL
L109        14562 S E7+NT
L110           20 S E9
                E MUSCULOSKELT/CT
                E MUSCULOSKELET/CT
L111        92613 S E5+NT
                E OSTEOARTHRIT/CT
                E E4+ALL
L112         2777 S E11,E12,E10+NT
                E MYALGIA/CT
                E E3+ALL
L113          118 S E2
                E LOCOMOTOR/CT
                E E6+ALL
L114           52 S E2
                E BONE METABOLISM/CT
                E METABOLISM/CT
L115           88 S E17 (L) BONE
L116        21427 S BONE (L) METABOL?
                E SPONDYLOS/CT
                E BONE, DISEASE/CT
L117        57335 S E3+NT
                E E21+ALL
L118          760 S E2
L119           41 S BONE, DISEASE/CT (L) SPONDYLO?
                E CHONDROLYS/CT
                E COLLAGENOSES/CT
                E COLLAGEN DISEASE/CT
                E E3+ALL
L120         2355 S E1,E2
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                E INFLAMMATION/CT
L121      72918 S E3+NT
                E ARTHROPATH/CT
                E E4+ALL
L122       1240 S E2
                E ARTHRITID/CT
L123      57335 S BONE, DISEASE+NT/CT
L124         11 S SPINAL COLUMN/CT (L) SPONDYLOS?
L125        169 S L90 AND L96-L124
L126          4 S L125 AND L85,L86

     FILE 'REGISTRY' ENTERED AT 17:41:41 ON 31 JAN 2003
L127          1 S 241475-68-3

     FILE 'HCAPLUS' ENTERED AT 17:41:46 ON 31 JAN 2003
L128          1 S L127 AND L90
                SEL DN AN L126 1 4
L129          2 S L126 AND E1-E6
L130          2 S L92,L129
L131          2 S L128,L130
L132        113 S L1 (L) (THU OR BAC)/RL AND L125
L133         32 S L132 NOT (?THROMB? OR ?COAGUL?)
L134        106 S L132 AND (1 OR 63)/SC,SX
                SEL DN AN 55 11 33 43 105
L135          5 S E7-E21
L136          6 S L131,L135 AND L73-L126,L128-L135
L137          5 S L136 NOT TUMOR/TI

     FILE 'HCAPLUS' ENTERED AT 17:50:25 ON 31 JAN 2003

     FILE 'EMBASE' ENTERED AT 17:50:39 ON 31 JAN 2003
L138       2859 S L3 OR L9
                E ENOXPARIN/CT
                E ENOXAPARIN/CT
                E E3+ALL
L139       2857 S E1 OR E1-E7/BI
L140       2862 S L138,L139
                E MUSCULOSKEL/CT
L141        259 S E6+NT AND L140
L142         27 S E22+NT AND L140
L143         75 S E23+NT AND L140
L144          0 S E36+NT AND L140
L145         24 S E48+NT AND L140
L146         21 S E53+NT AND L140
                E JOINT/CT
L147          6 S E3+NT AND L140
L148          0 S E35+NT AND L140
L149          0 S E60+NT AND L140
L150          0 S E74+NT AND L140
                E E 86+ALL
                E JOINT DISEASES/CT
                E E3+ALL
L151         79 S E2+NT AND L140
                E CONNECTIVE TISSUE/CT
L152          9 S E3+NT AND L140
L153         22 S E13+NT AND L140
                E WOUND/CT
L154         13 S (E3+NT OR E10+NT OR E14+NT) AND L140
L155          3 S (E29+NT OR E30+NT) AND L140
L156          3 S E37+NT AND L140
L157          3 S E52+NT AND L140
L158          3 S E81+NT AND L140
                E PERIODONT/CT
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L159          1 S E8+NT AND L140
L160          0 S E48+NT AND L140
                E BONE METABOLISM/CT
L161          3 S E3+NT AND L140
                E METABOLIC BONE/CT
L162        113 S E4+NT AND L140
                E LOCOMOTOR/CT
L163          0 S E8+NT AND L140
                E E11+ALL
L164         24 S E2+NT AND L140
L165        314 S L141-L164
L166        309 S L165 AND ENOXAPARIN/CT
L167         81 S L165 AND *ENOXAPARIN/CT
L168         31 S L167 NOT AB/FA
L169         50 S L167 NOT L168

     FILE 'WPIX' ENTERED AT 18:00:14 ON 31 JAN 2003
L170         22 S L3 OR L9
                SEL DN AN 8 19
L171          2 S L170 AND E1-E4

     FILE 'WPIX' ENTERED AT 18:01:33 ON 31 JAN 2003

     FILE 'EMBASE' ENTERED AT 18:01:44 ON 31 JAN 2003
                E MATRIX METALLOPROTEASE/CT
L172       3062 S E4+NT
L173       3140 S E4-E70
L174       4377 S E71+NT
L175        799 S E72-E108
L176       2226 S E109-E121
L177          3 S L140 AND L172-L176
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